Using the EuroQol EQ-5D in Swiss cancer patients, which value set should be applied?

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Abstract: BACKGROUND:The European Quality of Life-5 Dimensions (EQ-5D) instrument combines questionnaire responses into a single utility estimate using country-specific value sets. Countries without a national value set are advised to select one based on geographic proximity. In the absence of a Swiss value set, we used foreign value sets to gain insights into their appropriateness for use with Swiss cancer patients. METHODS: EQ-5D health states and visual analogue scale (VAS) ratings were collected in one German and three Swiss oncology trials. Utilities were calculated based on the United Kingdom (UK), German (GE), French (FR) and European Union (EU) value sets. Resulting differences and Pearson partial correlation coefficients with corresponding VAS ratings were assessed. RESULTS: In total, 202 Swiss and 154 German patients undergoing cancer treatment completed at least two EQ-5D forms. The mean difference between GE-based and FR-, UK- or EU-based utilities was significantly larger than the differences between the latter. The absolute mean difference between utilities and VAS ratings was highest for GE-based utilities, for Swiss (0.170, 95 % confidence interval [CI] 0.146-0.194) and German patients (0.174, 95 % CI 0.145-0.202). The correlation between GE-based utilities and VAS ratings was the lowest (r = 0.36, 95 % CI 0.33-0.40); the highest was between FR-based utilities and VAS ratings (r = 0.43, 95 % CI 0.39-0.46). CONCLUSION: For Switzerland, utility calculations based on the German or French value set would be an obvious choice. Our results suggest that the German value set may not be the most appropriate for use with Swiss cancer patients. The French and EU value sets may be relevant alternatives and improve international comparability.

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Using the EuroQol EQ-5D in Swiss cancer patients, which value set should be applied?

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Short running title:

The use of EuroQol EQ-5D in Swiss cancer patients

Abstract

Background

The European Quality of Life-5 Dimensions (EQ-5D) instrument combines questionnaire responses into a single utility estimate using country-specific value sets (VS). Countries without a national VS are advised to select a VS based on geographic proximity. In the absence of a Swiss VS we used foreign VS to gain insights into their appropriateness for use with Swiss cancer patients.

Methods

EQ-5D health states and visual analogue scale (VAS) ratings were collected in one German and three Swiss oncology trials. Utilities were calculated based on the United Kingdom (UK), German (GE), French (FR) and European Union (EU) VS. Resulting differences and Pearson partial correlation coefficients with corresponding VAS ratings were assessed.

Results

In total, 202 Swiss and 154 German patients undergoing cancer treatment completed at least 2 EQ-5D forms. The mean difference between GE-based and FR-, UK- or EU-based utilities was significantly larger than the differences between the latter. The absolute mean difference between utilities and VAS ratings was highest for GE-based utilities, for Swiss (0.170, 95%CI 0.146-0.194) and German patients (0.174, 95%CI 0.145-0.202). The correlation between GE-based utilities and VAS ratings was the lowest (r=0.36, 95%CI 0.33-0.40); the highest was between FR-based utilities and VAS ratings (r=0.43, 95%CI 0.39-0.46).

Conclusion

For Switzerland, utility calculations based on the German or French VS would be an obvious choice. Our results suggest that the German VS may not be the most appropriate for use with Swiss cancer patients. The French and European Union VS may be relevant alternatives and improve international comparability.

Keywords: EQ-5D, visual analogue scale, Switzerland, Germany, utility

Key points for decision makers

- In the absence of a national value set, the choice of a foreign value set for calculating EQ-5D utilities requires caution
- Compared to other European value sets the German value set may result in higher utilities
- Results of cost-utility calculations may be influenced by the chosen value set

Background

The European Quality of Life-5 Dimensions (EQ-5D) instrument [1] is widely used as a basis for estimating health state preferences (utilities). Results are typically used to calculate quality-adjusted life years (QALYs) in the context of cost-utility analysis. The EQ-5D questionnaire uses a descriptive system covering five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). There are three possible response categories for each, indicating no problems, some problems or severe problems, resulting in 243 possible health states. The instrument is complemented by a visual analogue scale (VAS) that allows individuals to rate their overall health state on a scale of 0 to 100. The VAS achieves a purely patient-based rating of health-related quality of life when used with clinical populations. In contrast, the responses to the EQ-5D questionnaire items are combined into a single utility estimate using country-specific scoring algorithms and value sets that are derived from general population-based time trade-off (TTO) or VAS studies [2, 3]. Patients' descriptions of real health states are thus combined with public preferences for hypothetical health states, in order to take into account societal preferences. Many studies have looked into the impact of different health state valuation methods or have provided cross-national comparisons of preference values [3-9], in order to ensure that comparability across countries is achieved [10]. Differences between the values assigned to health states in different countries are thought to be due to differences both in survey and analysis methods and in societal preferences and cultural differences. If no national value set is available for a given country the general advice is to select a value set based on geographic proximity [10]. However, value sets from foreign countries may not represent local societal values and can cause misleading results in cost-utility studies.

No Swiss value set exists to transform questionnaire-based EQ-5D health states reported by Swiss patients into utilities. The most obvious value sets to be used with Swiss patients would be the German [11] and French [12] ones, since Switzerland borders on both Germany and France. These two languages are spoken in different parts of Switzerland. Use of the European Union value set may be an alternative [13]. It is unclear, however, which of these foreign value sets would yield the most appropriate utility scores and best reflect Swiss culture.

In several oncology trials performed by the Swiss Group for Clinical Cancer Research (SAKK), as well as in a study conducted in German cancer patients, EQ-5D is part of the prospective health economic data collection. In the Swiss trials, patients with advanced breast cancer (SAKK 24/09), esophageal cancer (SAKK 75/08) or hepatocellular cancer (SAKK 77/08) were enrolled. The German trial (CESAR-TDM-C-III-002) enrolled patients with advanced lung cancer. In order to evaluate the impact of different value sets on utility estimates for these patients undergoing cancer treatment, we apply the German (TTO-based), French (TTO-based), United Kingdom (TTO-based) and European Union (VAS-based, study carried out in six Western European countries) value sets. The results achieved by applying the VAS based European Union value set are not based on choice under uncertainty and hence not utilities in a strict sense but, formally spoken, values or preferences [14]; for simplicity we still describe them as utilities in the context of this analysis. EQ-5D data from German patients were included to evaluate whether possible discrepancies between utilities calculated by applying the

various value sets to Swiss patients are a purely Swiss phenomenon or can also be observed in a German cancer patient population.

In the absence of a Swiss EQ-5D value set the overall aim of this study is to compare the application of four foreign value sets and to gain insights into their appropriateness for use with Swiss cancer patients.

Methods

So far, no methodology has been described that could serve as a basis for determining which foreign value set should be used to calculate country-specific utilities from questionnaire-based EQ-5D health states, if there is no national value set in place. In this study, we used a series of tentative approaches to compare the performance of different value sets. Utilities were calculated from patient-reported, questionnaire-based EQ-5D health states using the above-referenced candidate value sets. We subsequently assessed how the results differed from each other in terms of observed averages and how they were correlated. It was also assessed how they differed from the purely patient-based VAS ratings, and how they correlated with these [15]. The assumption behind this approach was that minor differences between utility scores resulting from different value sets and high correlations would indicate comparable valuations. Similar differences and correlations between utilities resulting from different value sets and VAS ratings would indicate a similar relationship with VAS ratings and hence a higher degree of agreement and interchangeability of value sets.

Patients

EQ-5D questionnaires were completed and VAS ratings were provided by patients enrolled in one German and three Swiss clinical cancer trials. The first Swiss trial involves advanced breast cancer patients receiving first-line treatment with chemotherapy and bevacizumab (SAKK 24/09, NCT01131195). It started in September 2010. The second Swiss trial involves patients with locally advanced esophageal cancer treated with chemotherapy (with or without cetuximab), radiotherapy and surgery (SAKK 75/08, NCT01107639). It started in May 2009. The third Swiss trial involves patients with advanced liver cancer (hepatocellular carcinoma) treated with sorafenib with or without everolimus (SAKK 77/08, NCT01005199). It started in December 2009. The German study involves advanced lung cancer patients treated with chemotherapy (Central European Society for Anticancer Research (CESAR) Study of Paclitaxel Therapeutic Drug Monitoring (CEPAC-TDM), NCT01326767). It started in March 2011. Patients completed the EQ-5D according to the clinical visit schedule of each study. An EQ-5D data extraction was made at the end of October 2012 while all studies were still ongoing. Data to be used for the present study included all fully completed forms; incomplete forms (with one or more questions not answered or VAS item missing) were excluded. In addition, only forms of patients who had completed a minimum of 2 forms were included in the analyses.

Data preparation and statistical analyses

For each completed EQ-5D questionnaire, utilities were calculated using the German (EQGE utility), European Union (EQEU utility), French (EQFR utility), and United Kingdom (EQUK utility) value sets

and calculation algorithms as described elsewhere. VAS ratings (ranging from 0 to 100) were divided by 100 in order to bring them to the same scale as used for the utility scores.

Descriptive statistics were performed to describe mean age of patients and number of completed EQ-5D forms per trial for both genders. The distribution of answer categories per questionnaire item was also analyzed. The distribution of utilities and VAS ratings was shown in turnip plots.

A mean EQ-5D utility per value set and a mean VAS score were calculated for every single patient. Thereafter, differences between mean utilities (EQGE-EQFR, EQGE-EQUK, EQGE-EQEU, etc.) and between mean utility and VAS score (EQGE-VAS, EQUK-VAS, EQFR-VAS etc.) were computed. These differences were assessed for statistical significance using a global linear mixed model controlling for gender, age and trial (only Swiss patients), with patients treated as a random factor. This analysis was performed separately for Swiss and German patients. Results were reported as predicted least square means (see Electronic Supplementary Material).

Pearson correlations between the utilities resulting from the different value sets and the VAS ratings were also calculated. To control for gender, age and trial (also covering cancer type) utilities and VAS ratings were also modelled using a mixed linear model with patients treated as a random factor and repeated measures for forms (controlling for the effect of patients clustered within trials). Subsequently the computed residuals for each utility and VAS were correlated. Pearson's correlation coefficients as well as Fischer's 95% confidence intervals were computed.

All analyses were performed using SAS® version 9.2, SAS Institute, Cary, NC.

Results

Patients

From May 2010 to October 2012 a total of 356 patients (202 (56.7%) Swiss and 154 (43.3%) German) in four different trials completed at least 2 EQ-5D forms (see table 1). The mean age of all patients was 62 years (standard deviation=9.4, Min-Max=24-85). On average, patients completed 6.2 forms (standard deviation=3.3, Min-Max=2-22); the study that had started first (SAKK77/08) had the highest average number of completed forms (8.7). More male (59%) than female patients (41%) were included.

Utilities and VAS ratings

The EQ-5D dimension most often reported to be impaired in the study populations was "Pain and Discomfort". In over 50% of the forms, the response categories of moderate or extreme pain or discomfort were used. The second most impaired dimension was anxiety and depression with almost 35% of the forms using the response categories representing moderately to extremely anxious or depressed (see figure 1). Some problems with daily activity were reported in 30% of all forms.

Patients from trial SAKK 75/08 (oesophageal cancer) showed the highest mean utilities (EQGE 0.92, 95%CI 0.90-0.94, to EQEU 0.83, 95%CI 0.81-0.86) and VAS ratings (0.76, 95%CI 0.73-0.79); patients

from trial SAKK 77/08 (liver cancer) showed the lowest utilities (EQGE 0.83, 95%CI 0.79-0.88, to EQEU 0.71, 95%CI 0.66-0.76) and VAS ratings (0.66, 95%CI 0.61-0.70). No large differences were observed between male and female patients (see table 2).

The overall mean utility (over all forms and patients) was at least 0.1 higher for the EQGE (0.87, 95%CI 0.85-0.88) value set compared to the EQUK (0.77, 95%CI 0.75-0.79), EQFR (0.77, 95%CI 0.74-0.79) and EQEU (0.76, 95%CI 0.75-0.78) value sets. The average VAS score (0.69, 95%CI 0.67-0.71) was 0.18-0.08 lower than the respective utility scores (table 2, figure 2).

Differences between utilities based on German, French, European Union and United Kingdom value sets

For the Swiss patients, differences between EQGE-EQFR, EQGE-EQUK and EQGE-EQEU utilities were significantly greater than differences between EQUK-EQEU, EQUK-EQFR or EQEU-EQFR utilities. The greatest difference was seen for EQGE-EQEU (0.107, 95%CI 0.098-0.116). In addition, the EQFR-EQEU difference was significantly greater than the EQFR-EQUK difference (see Electronic Supplementary Material). In the Swiss patients, the results were significantly influenced by trial (p=0.0003, estimate SAKK75/08 vs SAKK 77/08=-0.02510, estimate SAKK24/09 vs SAKK 77/08=-0.03048), gender (p=0.0246, estimate female vs male=0.02534) and age (p=0.0005, estimate=-0.00078 per additional year of age). Comparable results were seen for German patients. Marked differences were seen between EQGE and EQFR of 0.116 (95%CI 0.104-0.127), EQGE and EQUK of 0.106 (95%CI 0.095-0.118) and EQGE and EQEU of 0.111 (95%CI 0.099-0.122) utility scores, whereas differences for EQFR, EQUK and EQEU utility scores were close to zero and non-significant (see Figure 3). In the German patients only gender (p=0.036, estimate female versus male=0.01464) showed a significant effect.

Correlation between utilities based on German, French, European Union and United Kingdom value sets

Correlations between utilities based on the German, French, European Union and United Kingdom value sets were calculated on the basis of unadjusted results (without correcting for potential confounding by gender, age and clinical trial) as well as regression residuals resulting from the mixed linear model correcting for gender, age and clinical trial. In both cases, the EQGE utility scores showed the lowest correlation with EQFR (regression method: 0.87, 95%CI 0.861 – 0.881) and EQEU utility scores (regression method: 0.87, 95%CI 0.861 – 0.881). Highest correlations were seen between EQUK and EQGE (regression method: 0.96, 95%CI 0.954 – 0.961) and EQUK and EQEU (regression method: 0.96, 95%CI 0.965 – 0.970) scores (see Figure 4).

Differences between utilities based on German, French, European Union and United Kingdom value sets and VAS ratings

Overall VAS ratings were lower than the utilities calculated using the various value sets. Analysis of differences between VAS and utility scores using a global linear mixed model showed that the difference was greatest between EQGE utilities and VAS for Swiss patients (0.170, 95%CI 0.146-

0.194). This difference was significantly greater than for the EQFR (0.077, 95%CI 0.053-0.101), EQUK (0.074, 95%CI 0.050 – 0.098,) or EQEU (0.067, 95%CI 0.043-0.091,) utilities (see Figure 3). For Swiss patients, the trial, gender and age had no significant effect on the results. Similar results were seen for the German patients. The difference between the EQGE utilities and VAS for German patients was 0.174 (95%CI 0.145 – 0.202) and was significantly greater than that observed for VAS and EQFR-utility scores (0.061, 95%CI 0.033-0.089), VAS and EQUK utility scores (0.070, 95%CI 0.042-0.099) and VAS and EQEU utility scores (0.066, 95%CI 0.038-0.094). For German patients, only gender (p=0.048, female vs male estimate = -0.05564) showed a significant effect.

Correlation between utilities and VAS ratings

Correlations between the EQGE, EQFR, EQUK and EQEU utilities and VAS ratings were calculated on the basis of unadjusted results and regression residuals as described above. The unadjusted correlation coefficient for the EQGE utility with VAS scores (0.45, 95%CI 0.41-0.48) was significantly lower than EQFR (0.55, 95%CI 0.52-0.58), EQUK (0.51, 95%CI 0.48-0.54) and EQEU utilities (0.54, 95%CI 0.51-0.57) with VAS scores. After controlling for gender, age and trial, the correlation coefficients were about 0.1 lower and no significant differences between the individual value sets were observed (see figure 3). However the EQGE / VAS correlation coefficient (0.36, 95%CI 0.33-0.40) was again lowest and the EQFR/VAS correlation coefficient (0.43, 95%CI 0.39-0.46) was highest.

Discussion

In the absence of a Swiss EQ-5D value set we have estimated questionnaire-based EQ-5D utilities for Swiss and German cancer patients participating in one of four clinical oncology trials using the German, French, European Union and United Kingdom value sets. For countries without an own national value set the EuroQol group recommends the use of a value set based on geographic proximity. Therefore, in the case of Switzerland, the German [11] or French [12] value sets may be considered. However, as almost 23% (2011) of the population living permanently in Switzerland are foreigners, most of whom come from other European countries, the European Union [13] value set may also be considered. In the absence of a clear decision criterion and with implications for health economic analysis in mind, the aim of our study was to compare the application of the available value sets to questionnaire-based EQ-5D data and VAS ratings from Swiss patients.

Utilities based on the German value set are on average 0.1 higher than utilities based on the French, European Union or United Kingdom value sets, whereas the differences between the latter are all close to zero. This was observed for both Swiss and German patients. Heijnk et al.[5] have reported that the German value set generates higher quality-adjusted life years in summary measures of population health than the United Kingdom value set. Furthermore Gunther et al. [16] showed that, for patients with depression, utilities calculated with the German value set are higher than those calculated with the United Kingdom value set. Stark et al. also reported higher utility scores resulting from the German value set versus the United Kingdom value set in German inflammatory bowel disease patients [17]. These observations may indicate that differences between EQGE and EQUK utilities are disease independent. Our results show that, for cancer patients from both Switzerland and

Germany, utilities calculated with the German value set are higher than those calculated with the French, European Union or United Kingdom value sets. One reason may be that the cancer patients included in this study often reported that they had “some problems with daily activities” or were “unable to perform daily activities”, which in the German value set has no direct impact on the resulting utility. In addition, the response category “I am moderately anxious or depressed” is used in one third of the forms; this also has no impact on utility when the German value set is used. Therefore, it can be questioned whether the German value set is generally suitable for cancer patients. The two cancer-relevant dimensions of daily activity (impaired by tiredness) and anxiety/depression have only a minimal impact when this value set is used.

For both Swiss and German cancer patients, the difference between utilities based on the German value set and VAS ratings (0.172) is more than 0.1 greater than that between the utilities based on the other 3 value sets and VAS ratings (0.069). That VAS ratings in a general population render lower scores than valuations based on the time trade-off method has been described by Badia et al. [18]. In a review study, Pickard et al.[19] report the same phenomenon for cancer patients, who showed lower VAS ratings than EQ-5D utilities across all reviewed cancer studies. For patients with diabetes or chronic obstructive pulmonary disease [20], similar findings have been described, with VAS ratings lower than utilities. VAS ratings higher than utilities have been reported for inflammatory bowel syndrome patients [17]. Our results are in agreement with these observations; however, to the best of our knowledge we are the first to show that the magnitude of the differences between utility and VAS scores may heavily depend on the value set used to calculate the EQ-5D utility scores.

Whynes et al describe a correspondence between questionnaire-based EQ-5D utilities calculated with the United Kingdom value set and VAS ratings [15]. However, so far, there has been no direct comparison of the correlations between questionnaire-based EQ-5D utilities calculated with different value sets, and VAS ratings. Our results show that correlations between VAS ratings and questionnaire-based EQ-5D utilities depend on the value set used. In our case, use of the German value set results in the lowest correlation. The EQFR, EQEU and EQUK utilities all show a similar correlation with VAS ratings. It is clear that higher correlations and degree of similarity between questionnaire-based EQ-5D utilities and VAS ratings cannot be interpreted as a per se indicator of better suitability of a value set, due to the conceptual differences between the two types of measures [15, 21]. Nonetheless, Whyne et al. [15] found that EQ VAS scores are predictable from EQ-5D health state classifications”, indicating that some degree of correlation can be expected. The deviant result for the EQGE utilities therefore indicates a need for caution and further scrutiny.

The fact that all these phenomena are seen for both Swiss and German patients suggests that the German value set and algorithm itself rather than national/cultural differences may cause the issues described. The German value set was developed with a relatively small sample of the German population (n=334) compared to the United Kingdom (n=3395). This might have led to non-significant regression results for the above mentioned dimensions in the validation process. It would be of interest to verify the robustness of these results in a larger study.

Our study has some weaknesses to be considered. It is based on cancer patients (on active treatment) only. Whether or not a study of Swiss patients with other diseases would give similar results is unknown and should be the subject of future research. Switzerland has three major language regions (German, French and Italian) and the Swiss patients could choose which language form they preferred to complete given their spoken or best understood language. In our study we did not control for this language effect. Such linguistic complexity may make it more difficult to choose an appropriate foreign value set for Swiss patients. Should the French-speaking part of the population be valued with the French value set, as proposed by Perneger et al. [22], and the German-speaking population with the German value set? And what about Italian-speaking patients? A study that involves completion of the EQ-5D questionnaire by a representative general population sample from all over Switzerland might help to address this issue. The development of a Swiss value set could also be considered but may be impeded by the fact that Switzerland is a small country with 4 language regions and relevant cultural differences. Switzerland also has a large foreign population (about 23% in 2012). The development of the EQ5D-5L questionnaire, with a standardized study design to elicit value sets in different countries, may improve international comparability. However, this will not necessarily solve the issue of country specific differences and uncertainty in situations where no local value set exists. .

Conclusion

Although use of the German value set leads to outlying results in comparison with the French, European Union and United Kingdom value sets, there is no gold standard or decision criterion available that would allow us to make a finite statement on the suitability of the different datasets. We still see substantial hints that the German value set may not be the most suitable one for use with Swiss cancer patients. Depending on the anticipated analysis the French and European Union value sets are relevant alternatives and may improve international comparability.

In health economic evaluations based on the trials included here, using the German value set would lead to higher quality adjusted life time results than the French or European Union value sets. Situations might occur where cost-utility estimates would be biased towards the optimistic. In order to gauge incremental cost effectiveness ratios (ICER) in health economic studies alongside clinical trials in Swiss patients, one seems to be well advised to use utilities based on several value sets (and on VAS ratings to achieve a pure patient perspective). It is currently inappropriate to estimate the ICER and the corresponding level of cost effectiveness based on a single value set.

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Conflict of interest statement

The authors declare no conflict of interest.

Author's contribution

Klazien Matter-Walstra was the main responsible person for planning and conducting the study, performing statistics and writing the manuscript.

Dirk Klingbiel gave statistical support and reviewed the manuscript.

Matthias Schwenkglenks contributed to the planning of the study and interpretation of results, and reviewed the manuscript.

Thomas Szucs, Bernhard Pestalozzi gave support on content and reviewed the manuscript.

Table 1 Patient characteristics

			Age			Number of completed in forms		
		N	Mean STDEV	Median	Min-Max	Mean STDEV	Median	Min- Max
All		356	62.1 9.4	63.0	24-85	6.2 3.3	5	2-22
Trial	SAKK 24/09° breast cancer	92	59.9 12.2	62.5	24-83	6.8 3.8	6	2-20
	SAKK 75/08° esophageal cancer	72	63.2 7.6	63.0	42-77	6.7 2.2	6	3-12
	SAKK 77/08° Hepatocellular cancer	38	65.7 9.6	66.5	48-85	8.7 5.0	9	2-22
	CESAR C-III-002* lung cancer	154	62.1 7.9	62	40-77	5.1 2.3	5	2-11
Gender	Male	210	63.2 8.3	63	40-85	6.2 3.2	5	2-22
	Female	146	60.6 10.7	62	24-83	6.3 3.5	6	2-20

Legend: °=Swiss studies, *=German study, STDEV=standard deviation

Table 2 Mean VAS and EQ-5D utility scores

			VAS	Utility EQGE	Utility EQUK	Utility EQFR	Utility EQEU
		N	Mean Median (95%CI)	Mean Median (95%CI)	Mean Median (95%CI)	Mean Median (95%CI)	Mean Median (95%CI)
	All	356	0.69 0.71 (0.67-0.71)	0.87 0.9 (0.85-0.88)	0.77 0.79 (0.75-0.79)	0.77 0.82 (0.74-0.79)	0.76 0.77 (0.75-0.78)
Age	<50	34	0.70 0.71 (0.64-0.77)	0.87 0.88 (0.84-0.91)	0.75 0.73 (0.70-0.80)	0.76 0.8 (0.70-0.82)	0.74 0.72 (0.69-0.78)
	50-59	98	0.68 0.71 (0.64-0.72)	0.87 0.89 (0.85-0.89)	0.76 0.77 (0.73-0.79)	0.76 0.79 (0.72-0.79)	0.75 0.75 (0.72-0.78)
	60-69	137	0.69 0.72 (0.66-0.73)	0.86 0.92 (0.83-0.89)	0.77 0.82 (0.73-0.80)	0.77 0.84 (0.74-0.81)	0.77 0.80 (0.74-0.80)
	>69	87	0.69 0.70 (0.66-0.73)	0.87 0.89 (0.84-0.90)	0.78 0.82 (0.74-0.82)	0.77 0.83 (0.72-0.81)	0.77 0.80 (0.74-0.81)
Trial	SAKK 24/09 breast cancer	92	0.69 0.71 (0.65-0.73)	0.86 0.89 (0.83-0.89)	0.76 0.79 (0.72-0.80)	0.75 0.82 (0.70-0.80)	0.75 0.76 (0.71-0.79)
	SAKK 75/08 esophageal cancer	72	0.76 0.78 (0.73-0.79)	0.92 0.93 (0.90-0.94)	0.84 0.86 (0.81-0.87)	0.86 0.89 (0.83-0.89)	0.83 0.85 (0.81-0.86)
	SAKK 77/08 hepatocellular cancer	38	0.66 0.66 (0.61-0.70)	0.83 0.87 (0.79-0.88)	0.72 0.74 (0.66-0.77)	0.71 0.76 (0.64-0.78)	0.71 0.72 (0.66-0.76)
	CESAR C-III-002 lung cancer	154	0.67 0.69 (0.64-0.7)	0.85 0.89 (0.83-0.88)	0.75 0.76 (0.72-0.78)	0.74 0.78 (0.71-0.77)	0.75 0.75 (0.72-0.77)
Gender	Female	146	0.70 0.71 (0.67-0.73)	0.87 0.9 (0.84-0.89)	0.76 0.78 (0.73-0.79)	0.75 0.81 (0.72-0.79)	0.75 0.75 (0.72-0.77)
	Male	210	0.6 0.71 (0.67-0.71)	0.87 0.9 (0.85-0.88)	0.78 0.8 (0.75-0.80)	0.78 0.82 (0.75-0.81)	0.77 0.78 (0.75-0.79)
Country	Switzerland	202	0.71 0.73 (0.69-0.73)	0.88 0.91 (0.86-0.89)	0.78 0.81 (0.76-0.80)	0.78 0.84 (0.76-0.81)	0.77 0.79 (0.75-0.80)
	Germany	154	0.67 0.69 (0.64-0.70)	0.85 0.89 (0.83-0.88)	0.75 0.76 (0.72-0.78)	0.74 0.78 (0.71-0.77)	0.75 0.75 (0.72-0.77)

Legend: VAS=Visual analogue scale, EQGE=utility according to German value set, EQUK=utility according to United Kingdom value set, EQFR= utility according to French value set, EQEU= utility according to European Union value set

Figure 1 Percentage answers per question for the EQ-5D questionnaire

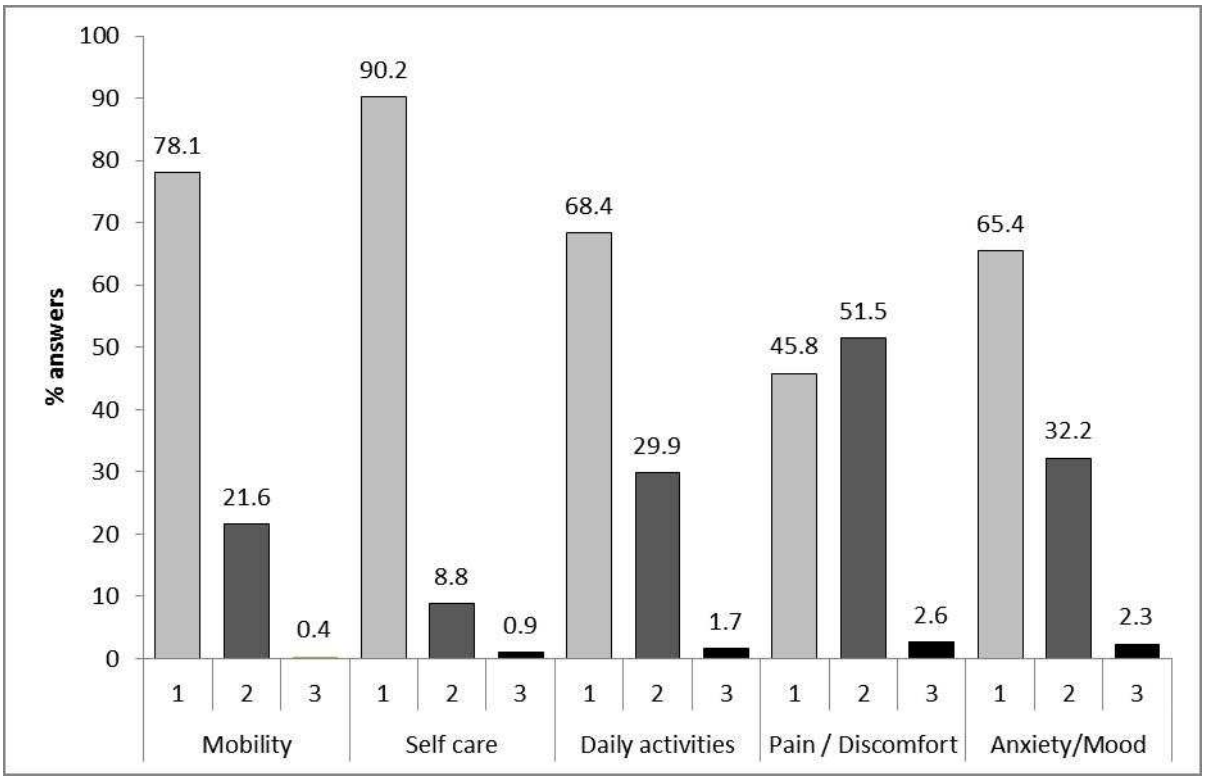
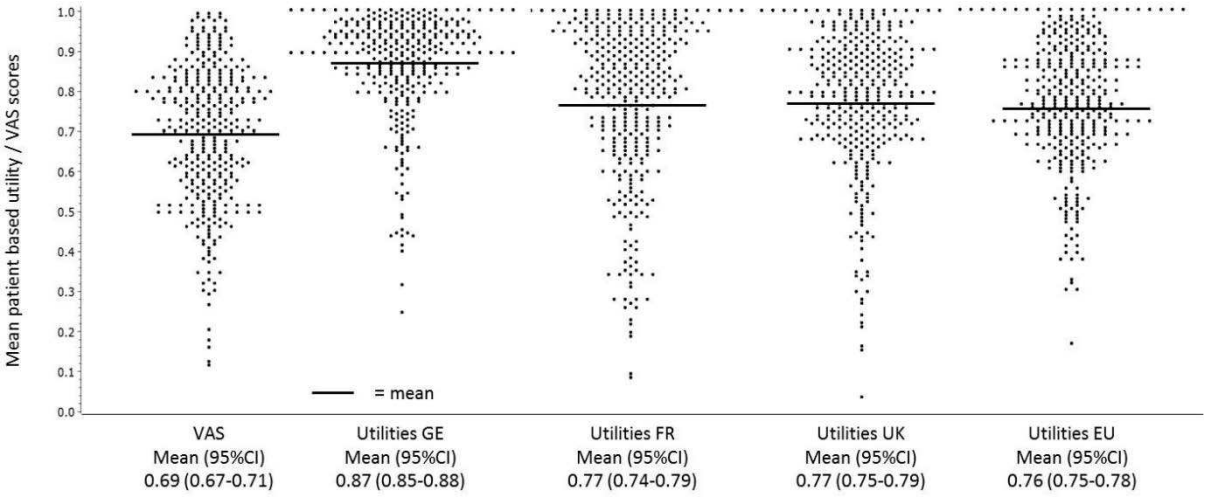
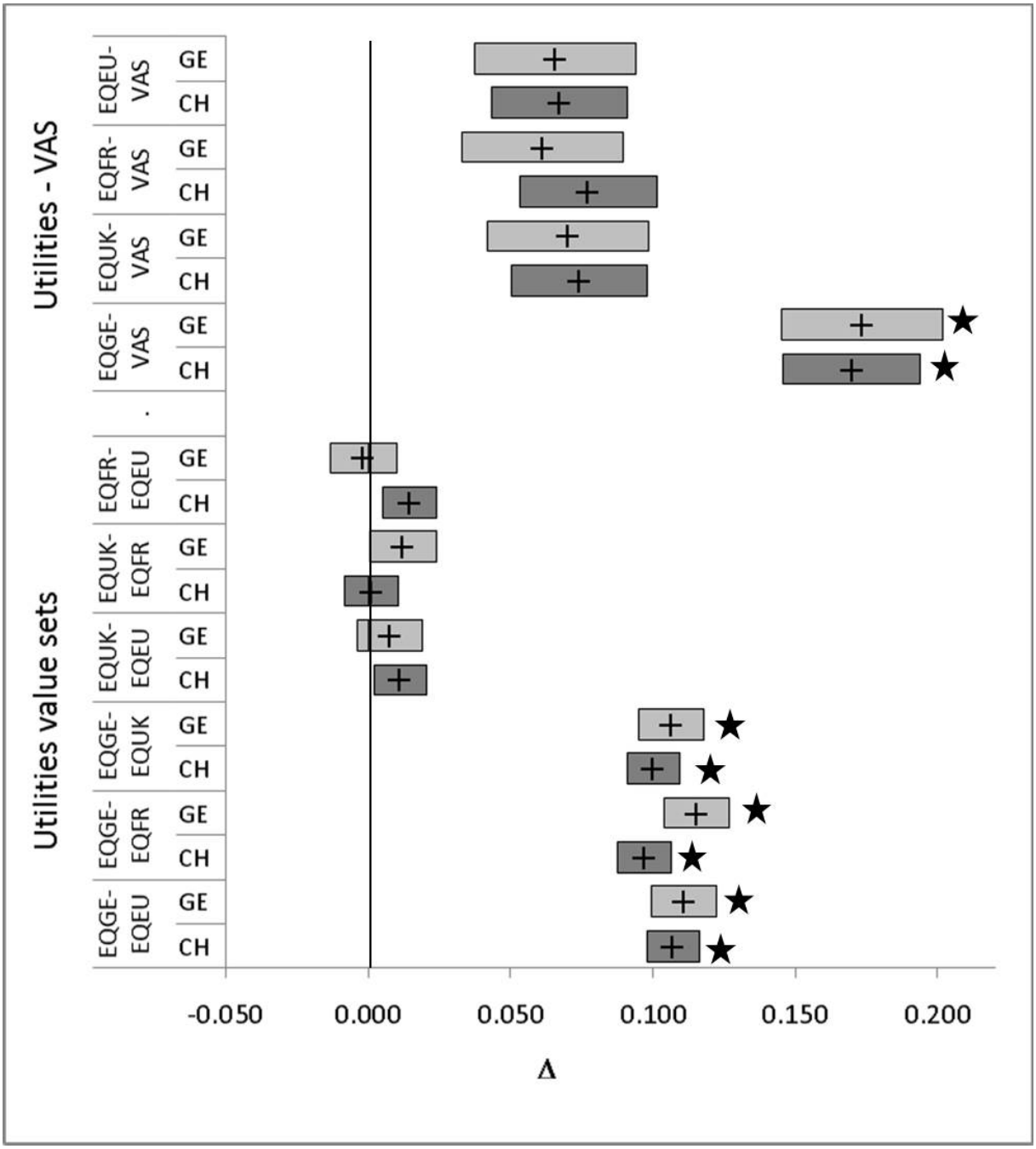


Figure 2 Turnip plots of average EQ-5D utility and VAS scores per patient



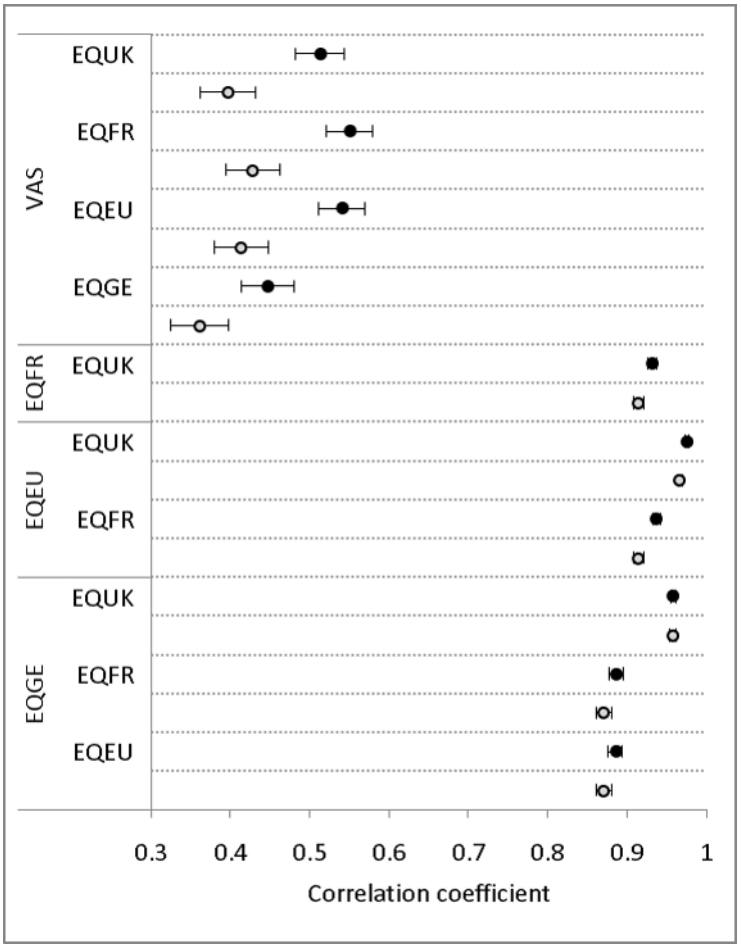
Legend: VAS=Visual analogue scale, GE=German value set, UK=United Kingdom value set, FR=French value set, EU= European Union value set

Figure 3 Differences between German, French, European Union and United Kingdom value set based EQ-5D utility scores and VAS and between utility scores for Swiss and German patients.



Legend: += least square mean, * significant, = 95%CI German patients, = 95%CI Swiss patients, VAS=Visual analogue scale, CH= Swiss, EQGE= utility according to German value set, EQUK= utility according to United Kingdom value set, EQFR= utility according to French value set, EQEU=utility according to European Union value set

Figure 4 Correlation of VAS and EQ-5D utilities according to GE, FR, UK and EU value sets



Legend: ● = correlation coefficient for raw data, ● = correlation coefficient for residual method, ├─┤ = 95% confidence interval, VAS=Visual analogue scale, EQGE= utility according to German value set, EQUK= utility according to United Kingdom value set, EQFR= utility according to French value set, EQEU=utility according to European Union value set

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